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 NEWS  2  AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS  3  OCT 07  EPFULL enhanced with full implementation of EPC2000
 NEWS  4  OCT 07  Multiple databases enhanced for more flexible patent
                  number searching
 NEWS  5  OCT 22  Current-awareness alert (SDI) setup and editing
                  enhanced
 NEWS  6  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS  7  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances
 NEWS  8  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  9  NOV 26  MARPAT enhanced with FSORT command
 NEWS 10  NOV 26  MEDLINE year-end processing temporarily halts
                  availability of new fully-indexed citations
 NEWS 11  NOV 26  CHEMSAFE now available on STN Easy
 NEWS 12  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS 13  DEC 01  ChemPort single article sales feature unavailable
 NEWS 14  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS 15  DEC 17  Fifty-one pharmaceutical ingredients added to PS

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              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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=> s (muscarinic(w)receptor or EGL(W)30 OR EGL(W)8 OR
guanine(w)nucleotide(w)binding(w)protein)
L1      139587 (MUSCARINIC(W) RECEPTOR OR EGL(W) 30 OR EGL(W) 8 OR GUANINE(W)
               NUCLEOTIDE(W) BINDING(W) PROTEIN)

=> l1 and inhibit
L1 IS NOT A RECOGNIZED COMMAND
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=> s l1 and (inhibit or alter)
L2       18404 L1 AND (INHIBIT OR ALTER)

=> s l2 and nematode
L3          45 L2 AND NEMATODE

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           30 DUP REM L3 (15 DUPLICATES REMOVED)

=> dis ibib abs l4 1-30

L4   ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:602744  CAPLUS
DOCUMENT NUMBER:          149:99802
TITLE:                    Regulated Trafficking of the MSP/Eph Receptor during
                          Oocyte Meiotic Maturation in C. elegans
AUTHOR(S):                Cheng, Hua; Govindan, J. Amaranath; Greenstein, David
CORPORATE SOURCE:         Department of Genetics, Cell Biology and Development,
                          University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE:                   Current Biology (2008), 18(10), 705-714
                          CODEN: CUBLE2; ISSN: 0960-9822
PUBLISHER:                Cell Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   In C. elegans, a sperm-sensing mechanism regulates oocyte meiotic
     maturation and ovulation, tightly coordinating sperm availability and
     embryo production; sperm release the major sperm protein (MSP) signal to
     trigger meiotic resumption.  Meiotic arrest depends on the parallel
     function of the oocyte VAB-1 MSP/Eph receptor and somatic G protein
     signaling.  MSP promotes meiotic maturation by antagonizing Eph receptor
     signaling and counteracting inhibitory inputs from the gonadal sheath
     cells.  Here, the authors present evidence suggesting that in the absence
     of the MSP ligand, the VAB-1 Eph receptor inhibits meiotic
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maturation while either in or in transit to the endocytic-recycling compartment. VAB-1::GFP localization to the RAB-11-pos. endocytic-recycling compartment is independent of ephrins but is antagonized by MSP signaling. Two neg. regulators of oocyte meiotic maturation, DAB-1/Disabled and RAN-1, interact with the VAB-1 receptor and are required for its accumulation in the endocytic-recycling compartment in the absence of MSP or sperm (hereafter referred to as MSP/sperm). Inactivation of the endosomal recycling regulators rme-1 or rab-11.1 causes a vab-1-dependent reduction in the meiotic-maturation rate in the presence of MSP/sperm. Further, the authors show that Gαs signaling in the gonadal sheath cells, which is required for meiotic maturation in the presence of MSP/sperm, affects VAB-1::GFP trafficking in oocytes. Regulated endocytic trafficking of the VAB-1 MSP/Eph receptor contributes to the control of oocyte meiotic maturation in C. elegans. Eph receptor trafficking in other systems may be influenced by the conserved proteins DAB-1/Disabled and RAN-1 and by crosstalk with G protein signaling in neighboring cells.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 30 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2008:414424 BIOSIS

DOCUMENT NUMBER: PREV200800414423

TITLE: Role of muscarinic 3 receptors in the immune, epithelial, and smooth muscle responses to enteric nematode infection.

AUTHOR(S): McLean, Leon P.; Zhao, Aiping; Sun, Rex; Stiltz, Jennifer A.; Riera, Diana C.; Urban, Joseph F.; Raufman, Jean-Pierre; Shea-Donohue, Terez

SOURCE: Gastroenterology, (APR 2008) Vol. 134, No. 4, Suppl. 1, pp. A393.
Meeting Info.: Digestive Disease Week Meeting/109th Annual Meeting of the American-Gastroenterological-Association. San Diego, CA, USA. May 17 -22, 2008. Amer Gastroenterol Assoc.
CODEN: GASTAB. ISSN: 0016-5085.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Jul 2008
Last Updated on STN: 31 Jul 2008

AB There is mounting evidence to support an anti-inflammatory role for vagal release of acetylcholine acting at nicotinic receptors on immune cells such as macrophages. Recent studies also demonstrate expression of muscarinic receptors (MR) on T cells, macrophages and dendritic cells (Kawashima et al., Life Sci, 2007) supporting a role for these receptors to the cholinergic-mediated anti-inflammatory pathway. M2R and M3R are expressed in the gut with M2R at a higher density; however, M3R mediate the direct effects of cholinergic agonists on smooth muscle and epithelial cells. There are new data indicating an immune regulation of MR activation (Akiho et al., AJP, 2007) Aim: To determine the contribution of M3R to nematode infection-induced immune response and changes in gut function. Methods: WT and M3R deficient KO mice were infected with Nippostrongylus brasiliensis (Nb)and studied 10 days later. Muscle-free sections of jejunum were placed microsnapwells to determine transepithelial electrical resistance (TEER), an index of mucosal permeability. Segments of jejunum were suspended in organ baths and smooth muscle responses to acetylcholine (ACH, 10 nM-0.1 mM) and electrical field stimulation (EFS, 1-20HZ, 80V) were determined. Real-time PCR was used to measure mRNA expression of cytokines and MRs. Results: As reported previously, Nb infection significantly increased IL-13 and IL-4 expression, enhanced responses of smooth muscle to ACH and

EFS, and reduced epithelial resistance (data not shown). Nb also significantly upregulated mRNA expression of M3R (1. +/- 0.1 vs 3.5 +/- 3.3 fold),but did not alter expression of M2R or MIR. In M3RKO mice, Th2 cytokine expression was upregulated (Table). Surprisingly, there was also and upregulation of IFN gamma, NOS-2 (table), and IL-17A (20 fold), genes that are normally unaltered or suppressed during Nb infection. The infection induced drop in TEER and the hypercontractility to ACH was similar to that WT mice. In contrast, the infection induced hyper-responsiveness to nerve stimulation was absent in M3RKO mice. Conclusions: These data show infection-induced hypercontractility to ACH is maintained in M3RKO mice and this likely reflects compensation by M2R. M3R does not alter Nb-induced increase in permeability, but is important for the hypersensitivity to EFS. Of interest, M3R may also contribute to the modulation of the balance of Th1/Th2/Th17 cytokines during infection.[GRAPHICS]

L4 ANSWER 3 OF 30 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2008050894 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17942636
TITLE: Intestinal Ca2+ wave dynamics in freely moving C. elegans coordinate execution of a rhythmic motor program.
AUTHOR: Nehrke K; Denton Jerod; Mowrey William
CORPORATE SOURCE: Dept. of Medicine, Nephrology Division, Medical Center Box 675, 601 Elmwood Ave., Rochester NY 14642, USA.. keith_nehrke@urmc.rochester.edu
CONTRACT NUMBER: R01 HL-080810 (United States NHLBI)
R21 DK-071645 (United States NIDDK)
T32 MH-065181 (United States NIMH)
SOURCE: American journal of physiology. Cell physiology, (2008 Jan) Vol. 294, No. 1, pp. C333-44. Electronic Publication: 2007-10-17.
Journal code: 100901225. ISSN: 0363-6143.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200802
ENTRY DATE: Entered STN: 23 Jan 2008
Last Updated on STN: 22 Feb 2008
Entered Medline: 21 Feb 2008

AB Defecation in the nematode worm Caenorhabditis elegans is a highly rhythmic behavior that is regulated by a Ca(2+) wave generated in the 20 epithelial cells of the intestine, in part through activation of the inositol 1,4,5-trisphosphate receptor. Execution of the defecation motor program (DMP) can be modified by external cues such as nutrient availability or mechanical stimulation. To address the likelihood that environmental regulation of the DMP requires integrating distinct cellular and organismal processes, we have developed a method for studying coordinate Ca(2+) oscillations and defecation behavior in intact, freely behaving animals. We tested this technique by examining how mutations in genes known to alter Ca(2+) handling [including egl-8/phospholipase C (PLC)-beta, kqt-3/KCNQ1, sca-1/sarco(endo)plasmic reticulum Ca(2+) ATPase, and unc-43/Ca(2+)-CaMKII] contribute to shaping the Ca(2+) wave and asked how Ca(2+) wave dynamics in the mutant backgrounds altered execution of the DMP. Notably, we find that Ca(2+) waves in the absence of PLCbeta initiate ectopically, often traveling in reverse, and fail to trigger a complete DMP. These results suggest that the normal supremacy of the posterior intestinal cells is not obligatory for Ca(2+) wave occurrence but instead helps to coordinate the DMP. Furthermore, we present evidence suggesting that an underlying pacemaker appears to oscillate at a faster

frequency than the defecation cycle and that arrhythmia may result from uncoupling the pacemaker from the DMP rather than from disrupting the pacemaker itself. We also show that chronic elevations in Ca(2+) have limited influence on the defecation period but instead alter the interval between successive steps of the DMP. Finally, our results demonstrate that it is possible to assess Ca(2+) dynamics and muscular contractions in a completely unrestrained model organism.

L4 ANSWER 4 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2008041182 EMBASE
TITLE: Intestinal Ca(2+) wave dynamics in freely moving C. elegans coordinate execution of a rhythmic motor program.
AUTHOR: Nehrke, K. (correspondence)
CORPORATE SOURCE: Nephrology Division, Department of Medicine, University of Rochester Medical Center, Rochester, NY, United States. keith_nehrke@urmc.rochester.edu
AUTHOR: Denton, Jerod
CORPORATE SOURCE: Departments of Anesthesiology and Pharmacology, Digestive Disease Research Center, Vanderbilt University Medical Center, Nashville, TN, United States.
AUTHOR: Mowrey, William
CORPORATE SOURCE: Interdepartmental Graduate Program in Neuroscience, Center for Aging and Developmental Biology, University of Rochester Medical Center, Rochester, NY, United States.
AUTHOR: Nehrke, K. (correspondence)
CORPORATE SOURCE: Dept. of Medicine, Nephrology Division, Medical Center Box 675, 601 Elmwood Ave., Rochester, NY 14642, United States. keith_nehrke@urmc.rochester.edu
SOURCE: American Journal of Physiology - Cell Physiology, (Jan 2008) Vol. 294, No. 1, pp. C333-C344.
Refs: 39
ISSN: 0363-6143 E-ISSN: 1522-1563 CODEN: AJPCDD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Feb 2008
Last Updated on STN: 18 Feb 2008

AB Defecation in the nematode worm Caenorhabditis elegans is a highly rhythmic behavior that is regulated by a Ca(2+) wave generated in the 20 epithelial cells of the intestine, in part through activation of the inositol 1,4,5-trisphosphate receptor. Execution of the defecation motor program (DMP) can be modified by external cues such as nutrient availability or mechanical stimulation. To address the likelihood that environmental regulation of the DMP requires integrating distinct cellular and organismal processes, we have developed a method for studying coordinate Ca(2+) oscillations and defecation behavior in intact, freely behaving animals. We tested this technique by examining how mutations in genes known to alter Ca(2+) handling [including egl-8/phospholipase C (PLC)-β, kqt-3/KCNQ1, sca-1/sarco (endo)plasmic reticulum Ca(2+) ATPase, and unc-43/Ca (2+)-CaMKII] contribute to shaping the Ca(2+) wave and asked how Ca(2+) wave dynamics in the mutant backgrounds altered execution of the DMP. Notably, we find that Ca(2+) waves in the absence of PLCβ initiate ectopically, often traveling in reverse, and fail to trigger a complete DMP. These results suggest that the normal supremacy of the posterior intestinal cells is not obligatory for Ca(2+) wave occurrence but instead helps to coordinate the DMP. Furthermore, we present evidence suggesting that an underlying pacemaker appears to oscillate at a faster frequency than the defecation

cycle and that arrhythmia may result from uncoupling the pacemaker from the DMP rather than from disrupting the pacemaker itself. We also show that chronic elevations in Ca(2+) have limited influence on the defecation period but instead alter the interval between successive steps of the DMP. Finally, our results demonstrate that it is possible to assess Ca (2+) dynamics and muscular contractions in a completely unrestrained model organism.

L4 ANSWER 5 OF 30 CAPLUS
ACCESSION NUMBER: 2007:818025 CAPLUS
DOCUMENT NUMBER: 147:228752
TITLE: Controlling pests using RNA interference targeted toward essential genes of insects
INVENTOR(S): Raemaekers, Romaan; Feldmann, Pascale; Plaetinck, Geert; Nooren, Irene; Van Bleu, Els; Pecqueur, Frederic; Kubler, Laurent; Damme, Nicole; Degrave, Lies; Remory, Isabel
PATENT ASSIGNEE(S): Devgen NV, Belg.
SOURCE: PCT Int. Appl., 360pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007083193	A2	20070726	WO 2006-IB4008	20060918
WO 2007083193	A3	20080124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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AU 2006335978	A1	20070726	AU 2006-335978	20060918
CA 2622671	A1	20070726	CA 2006-2622671	20060918
EP 1934357	A2	20080625	EP 2006-849359	20060918
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MX 200803649	A	20080624	MX 2008-3649	20080314

PRIORITY APPLN. INFO.:

US 2005-718034P	P	20050916
US 2006-758191P	P	20060112
US 2006-771160P	P	20060207
US 2006-837910P	P	20060816
WO 2006-IB3446	A	20060915
WO 2006-IB4008	W	20060918

AB The present invention concerns methods for controlling insect infestation via RNAnucleotide interference (RNAi)-mediated gene silencing, whereby the intact insect cell(s) are contacted with a double-stranded RNA (dsRNA) from outside the insect cell(s) and whereby the double-stranded RNA is taken up by the intact insect cell(s). The sequence of the dsRNA corresponds to part or whole of an essential insect gene and causes down-regulation of the insect target via RNAi. Essential genes were

identified for Leptinotarsa decemlineata (Colorado potato beetle), Phaedon cochleariae (mustard leaf beetle), Anthonomus grandis (cotton boll weevil), Myzus persicae (green peach aphid), Chilo suppressalis (rice striped stem borer), Plutella xylostella (diamondback moth), Epilachna varivetis (Mexican bean beetle), Tribolium castaneum (red flour beetle), Nilaparvata lugens (brown plant hopper), and Acheta domesticus (house cricket). In addition, sequences orthologous to insect essential genes are provided for arachnida, nematode, and fungal species. The methods of the invention can find practical application in any area of technol. where it is desirable to inhibit viability, growth, development, or reproduction of the insect, or to decrease pathogenicity or infectivity of the insect. Suitable insect target genes and fragments thereof, dsRNA constructs, recombinant constructs, and compns. are disclosed.

L4 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:790098 CAPLUS
DOCUMENT NUMBER: 147:183063
TITLE: Controlling pests using RNA interference targeted toward essential genes of insects
INVENTOR(S): Raemaekers, Romaan; Kubler, Laurent; Plaetinck, Geert; Vanbleu, Els
PATENT ASSIGNEE(S): Devgen N.V., Belg.
SOURCE: PCT Int. Appl., 324pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007080127	A2	20070719	WO 2007-EP287	20070112
WO 2007080127	A3	20080327		
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CA 2627795	A1	20070719	CA 2007-2627795	20070112
EP 1971688	A2	20080924	EP 2007-700223	20070112
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MX 200808361	A	20080710	MX 2008-8361	20080625

PRIORITY APPLN. INFO.:

EP 2006-447008	A	20060112
US 2006-758191P	P	20060112
US 2006-771160P	P	20060207
US 2006-837910P	P	20060816
US 2006-875362P	P	20061218
WO 2007-EP287	W	20070112

AB The present invention concerns methods for controlling insect infestation via RNA interference (RNAi)-mediated gene silencing, whereby the intact insect cell(s) are contacted with a double-stranded RNA (dsRNA) from outside the insect cell(s) and whereby the double-stranded RNA is taken up

by the intact insect cell(s). The sequence of the dsRNA corresponds to part or whole of an essential insect gene and causes down-regulation of the insect target via RNAi. Essential genes were identified for Leptinotarsa decemlineata (Colorado potato beetle), Phaedon cochleariae (mustard leaf beetle), Anthonomus grandis (cotton boll weevil), Myzus persicae (green peach aphid), Chilo suppressalis (rice striped stem borer), Plutella xylostella (diamondback moth), Epilachna varivetis (Mexican bean beetle), Tribolium castaneum (red flour beetle), Nilaparvata lugens (brown plant hopper), and Acheta domesticus (house cricket). In addition, sequences orthologous to insect essential genes are provided for arachnida, nematode, and fungal species. The methods of the invention can find practical application in any area of technol. where it is desirable to inhibit viability, growth, development, or reproduction of the insect, or to decrease pathogenicity or infectivity of the insect. Suitable insect target genes and fragments thereof, dsRNA constructs, recombinant constructs, and compns. are disclosed.

L4 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:790448 CAPLUS
DOCUMENT NUMBER: 147:205873
TITLE: Controlling pests using RNA interference targeted toward essential genes of insects
INVENTOR(S): Raemaekers, Romaan; Kubler, Laurent; Vanbleu, Els
PATENT ASSIGNEE(S): Devgen N.V., Belg.
SOURCE: PCT Int. Appl., 297pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007080126	A2	20070719	WO 2007-EP286	20070112
WO 2007080126	A3	20080327		
WO 2007080126	A9	20080814		
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EP 1971687	A2	20080924	EP 2007-700222	20070112
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MX 200808403	A	20080710	MX 2008-8403	20080626

PRIORITY APPLN. INFO.:

EP 2006-447008	A	20060112
US 2006-758191P	P	20060112
US 2006-771160P	P	20060207
US 2006-837910P	P	20060816
US 2006-875356P	P	20061218
WO 2007-EP286	W	20070112

AB The present invention concerns methods for controlling insect infestation via RNA interference (RNAi)-mediated gene silencing, whereby the intact

insect cell(s) are contacted with a double-stranded RNA (dsRNA) from outside the insect cell(s) and whereby the double-stranded RNA is taken up by the intact insect cell(s). The sequence of the dsRNA corresponds to part or whole of an essential insect gene and causes down-regulation of the insect target via RNAi. Essential genes were identified for Leptinotarsa decemlineata (Colorado potato beetle), Phaedon cochleariae (mustard leaf beetle), Anthonomus grandis (cotton boll weevil), Myzus persicae (green peach aphid), Chilo suppressalis (rice striped stem borer), Plutella xylostella (diamondback moth), Epilachna varivetis (Mexican bean beetle), Tribolium castaneum (red flour beetle), Nilaparvata lugens (brown plant hopper), and Acheta domesticus (house cricket). In addition, sequences orthologous to insect essential genes are provided for arachnida, nematode, and fungal species. The methods of the invention can find practical application in any area of technol. where it is desirable to inhibit viability, growth, development, or reproduction of the insect, or to decrease pathogenicity or infectivity of the insect. Suitable insect target genes and fragments thereof, dsRNA constructs, recombinant constructs, and compns. are disclosed.

L4 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:532445 CAPLUS
DOCUMENT NUMBER: 147:114090
TITLE: An activating mutation in sos-1 identifies its Dbl domain as a critical inhibitor of the epidermal growth factor receptor pathway during Caenorhabditis elegans Vulval development
AUTHOR(S): Modzelewska, Katarzyna; Elgort, Marc G.; Huang, Jingyu; Jongeward, Gregg; Lauritzen, Amara; Yoon, Charles H.; Sternberg, Paul W.; Moghal, Nadeem
CORPORATE SOURCE: Department of Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 84112-5550, USA
SOURCE: Molecular and Cellular Biology (2007), 27(10), 3695-3707
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proper regulation of receptor tyrosine kinase (RTK)-Ras-mitogen-activated protein kinase (MAPK) signaling pathways is critical for normal development and the prevention of cancer. SOS is a dual-function guanine nucleotide exchange factor (GEF) that catalyzes exchange on Ras and Rac. Although the physiol. role of SOS and its CDC25 domain in RTK-mediated Ras activation is well established, the in the vivo function of its Dbl Rac GEF domain is less clear. The authors have identified a novel gain-of-function missense mutation in the Dbl domain of Caenorhabditis elegans SOS-1 that promotes epidermal growth factor receptor (EGFR) signaling in vivo. The authors' data indicate that a major developmental function of the Dbl domain is to inhibit EGF-dependent MAPK activation. The amount of inhibition conferred by the Dbl domain is equal to that of established trans-acting inhibitors of the EGFR pathway, including c-Cbl and RasGAP, and more than that of MAPK phosphatase. In conjunction with mol. modeling, the authors' data suggest that the C. elegans mutation, as well as an equivalent mutation in human SOS1, activates the MAPK pathway by disrupting an autoinhibitory function of the Dbl domain on Ras activation. The authors' work suggests that functionally similar point mutations in humans could directly contribute to disease.
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:691811 CAPLUS

DOCUMENT NUMBER: 147:162507
TITLE: Cortical centralspindlin and Gα have parallel roles in furrow initiation in early C. elegans embryos
AUTHOR(S): Verbrugghe, Koen J. C.; White, John G.
CORPORATE SOURCE: Laboratory of Genetics, University of Wisconsin - Madison, Madison, WI, 53706, USA
SOURCE: Journal of Cell Science (2007), 120(10), 1772-1778
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Evidence from various systems suggests that either asters or the midzone of the mitotic spindle are the predominant determinants of cleavage plane position. Disrupting spindle midzone formation in the one-cell Caenorhabditis elegans embryo, such as by using mutants of the centralspindlin component ZEN-4, prevents completion of cytokinesis but does not inhibit furrowing. However, furrowing is inhibited by the simultaneous depletion of ZEN-4 with either PAR-2 or Gα, which are required for asym. divisions. Through studies of other genes required for the presence of an intact spindle midzone containing microtubule bundles, the authors found that furrowing failed in the absence of PAR-2 or Gα only when centralspindlin was absent from the furrow. The authors also found spindle length or microtubule distribution did not correlate with furrow initiation. The authors propose that centralspindlin acts redundantly with Gα to regulate furrow initiation.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:976940 CAPLUS
DOCUMENT NUMBER: 147:361230
TITLE: Dopamine mediates context-dependent modulation of sensory plasticity in C. elegans
AUTHOR(S): Kindt, Katie S.; Quast, Kathleen B.; Giles, Andrew C.; De, Subhajyoti; Hendrey, Dan; Nicastro, Ian; Rankin, Catharine H.; Schafer, William R.
CORPORATE SOURCE: Biomedical Sciences Graduate Program, University of California, San Diego, La Jolla, CA, 92093, USA
SOURCE: Neuron (2007), 55(4), 662-676
CODEN: NERNET; ISSN: 0896-6273
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dopamine has been implicated in the modulation of diverse forms of behavioral plasticity, including appetitive learning and addiction. An important challenge is to understand how dopamine's effects at the cellular level alter the properties of neural circuits to modify behavior. In the nematode C. elegans, dopamine modulates habituation of an escape reflex triggered by body touch. In the absence of food, animals habituate more rapidly than in the presence of food; this contextual information about food availability is provided by dopaminergic mechanosensory neurons that sense the presence of bacteria. The authors find that dopamine alters habituation kinetics by selectively modulating the touch responses of the anterior-body mechanoreceptors; this modulation involves a D1-like dopamine receptor, a Gq/PLC-β signaling pathway, and calcium release within the touch neurons. Interestingly, the body touch mechanoreceptors can themselves excite the dopamine neurons, forming a pos. feedback loop capable of integrating context and experience to modulate mechanosensory attention.

REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007317202 EMBASE
TITLE: Genetics and the mechanisms of action of inhaled anesthetics.
AUTHOR: Steele, Louise M.; Morgan, Phil G. (correspondence); Sedensky, Margaret M.
CORPORATE SOURCE: Department of Genetics, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH 44106-5007, United States. philip.morgan@uhhospitals.org
AUTHOR: Morgan, Phil G. (correspondence); Sedensky, Margaret M.
CORPORATE SOURCE: Department of Anesthesiology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH 44106-5007, United States. philip.morgan@uhhospitals.org
AUTHOR: Morgan, Phil G. (correspondence)
CORPORATE SOURCE: Deparment of Pharmacology, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH 44106-5007, United States. philip.morgan@uhhospitals.org
AUTHOR: Morgan, Phil G. (correspondence)
CORPORATE SOURCE: Department of Anesthesiology, University Hospitals, Case Western Reserve University, Cleveland, OH 44106-5007, United States. philip.morgan@uhhospitals.org
SOURCE: Current Pharmacogenomics, (Jun 2007) Vol. 5, No. 2, pp. 125-141.
Refs: 153
ISSN: 1570-1603 CODEN: CPUHAC
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 022 Human Genetics
024 Anesthesiology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2007
Last Updated on STN: 17 Jul 2007

AB Inhaled anesthetics have been used for more than a century, and they are currently administered to millions of patients each year. Although well understood in an empirical sense, their basic molecular mechanisms of action are still unknown. During the past two decades, a large amount of evidence has been presented that is most consistent with the hypothesis that inhaled anesthetics act at multiple sites. For example, genetic mutations exist that distinguish between different inhaled anesthetics, i.e. the mutations alter sensitivity to some anesthetics differently than others. Since it is probable that multiple mechanisms contribute to inhaled anesthetic action, a genetic approach is a powerful method for sorting out which molecules are involved in specific anesthetic effects. This review describes recent pharmacogenetic studies performed using model organisms, including yeast, nematodes, fruit flies, and mice. At first glance, the results of these studies are notable for their lack of a common putative molecular target. In fact, the results suggest that anesthetics interact with a seemingly broad range of cellular components including ion channels, membrane receptors, lipid rafts, and the mitochondrial electron transport chain. However, a unifying theme is beginning to emerge, one that implicates the presynaptic neuron as a common functional target for inhaled anesthetics. Intriguing similarities among the results suggest that many of the findings obtained in model organisms can be generalized across disparate phyla, and that the findings will be applicable in humans. By continuing to exploit the power of genetics, such studies are likely to unravel the great mystery of how

inhaled anesthetics produce their effects. .COPYRGT. 2007 Bentham Science Publishers Ltd.

L4 ANSWER 12 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 2

ACCESSION NUMBER: 2007057837 EMBASE
TITLE: Delayed goblet cell hyperplasia, acetylcholine receptor expression, and worm expulsion in SMC-specific IL-4Rα-deficient mice.
AUTHOR: Horsnell, William G. C.; Cutler, Antony J.; Hoving, Claire J.; Mearns, Helen; Myburgh, Elmarie; Arendse, Berenice; Brombacher, Frank (correspondence)
CORPORATE SOURCE: Division of Immunology, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa. fbrombac@uctgshl.uct.ac.za
AUTHOR: Finkelman, Fred D.
CORPORATE SOURCE: Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, OH, United States.
AUTHOR: Owens, Gary K.
CORPORATE SOURCE: Department of Molecular Physiology and Biological Physics, University of Virginia Health Sciences Center, Charlottesville, VA, United States.
AUTHOR: Erle, Dave
CORPORATE SOURCE: Lung Biology Center, Department of Medicine, University of California San Francisco, San Francisco, CA, United States.
SOURCE: PLoS Pathogens, (Jan 2007) Vol. 3, No. 1, pp. 0046-0053. Refs: 35
ISSN: 1553-7366 E-ISSN: 1553-7374
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Mar 2007
Last Updated on STN: 15 Mar 2007

AB Interleukin 4 receptor a (IL-4Rα) is essential for effective clearance of gastrointestinal nematode infections. Smooth muscle cells are considered to play a role in the type 2 immune response-driven expulsion of gastrointestinal nematodes. Previous studies have shown in vitro that signal transducer and activator of transcription 6 signaling in response to parasitic nematode infection significantly increases smooth muscle cell contractility. Inhibition of the IL-4Rα pathway inhibits this response. How this response manifests itself in vivo is unknown. In this study, smooth muscle cell IL-4Rα-deficient mice (SM-MHC(Cre)IL-4Rα(-/lox)) were generated and characterized to uncover any role for IL-4/IL-13 in this non-immune cell type in response to Nippostrongylus brasiliensis infection. IL-4Rα was absent from α-actin-positive smooth muscle cells, while other cell types showed normal IL-4Rα expression, thus demonstrating efficient cell-type-specific deletion of the IL-4Rα gene. N. brasiliensis-infected SM-MHC(Cre)IL-4Rα(-/lox) mice showed delayed ability to resolve infection with significantly prolonged fecal egg recovery and delayed worm expulsion. The delayed expulsion was related to a delayed intestinal goblet cell hyperplasia, reduced T helper 2 cytokine production in the mesenteric lymph node, and reduced M3 muscarinic receptor expression during infection. Together, these results demonstrate that in vivo IL-4Rα-responsive smooth muscle cells are beneficial for N. brasiliensis expulsion by coordinating T helper 2 cytokine responses, goblet hyperplasia, and acetylcholine responsiveness,

which drive smooth muscle cell contractions. .COPYRGT. 2007 Horsnell et al.

L4 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:742084 CAPLUS
DOCUMENT NUMBER: 147:254167
TITLE: A role for Rab5 in structuring the endoplasmic reticulum
AUTHOR(S): Audhya, Anjon; Desai, Arshad; Oegema, Karen
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Department of Cellular and Molecular Medicine, University of California, San Diego, La Jolla, CA, 92093, USA
SOURCE: Journal of Cell Biology (2007), 178(1), 43-56
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The endoplasmic reticulum (ER) is a contiguous network of interconnected membrane sheets and tubules. The ER is differentiated into distinct domains, including the peripheral ER and nuclear envelope. Inhibition of two ER proteins, Rtn4a and DP1/NogoA, was previously shown to inhibit the formation of ER tubules in vitro. The authors show that the formation of ER tubules in vitro also requires a Rab family GTPase. Characterization of the 29 Caenorhabditis elegans Rab GTPases reveals that depletion of RAB-5 phenocopies the defects in peripheral ER structure that result from depletion of RET-1 and YOP-1, the C. elegans homologs of Rtn4a and DP1/NogoA. Perturbation of endocytosis by other means did not affect ER structure; the role of RAB-5 in ER morphol. is thus independent of its well-studied requirement for endocytosis. RAB-5 and YOP-1/RET-1 also control the kinetics of nuclear envelope disassembly, which suggests an important role for the morphol. of the peripheral ER in this process.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2007299228 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17222057
TITLE: Delayed goblet cell hyperplasia, acetylcholine receptor expression, and worm expulsion in SMC-specific IL-4Ralpha-deficient mice.
AUTHOR: Horsnell William G C; Cutler Antony J; Hoving J Claire; Hoving Claire J; Mearns Helen; Myburgh Elmarie; Arendse Berenice; Finkelman Fred D; Owens Gary K; Erle Dave; Brombacher Frank
CORPORATE SOURCE: Division of Immunology, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa.
SOURCE: PLoS pathogens, (2007 Jan) Vol. 3, No. 1, pp. e1.
Journal code: 101238921. E-ISSN: 1553-7374.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200706
ENTRY DATE: Entered STN: 22 May 2007
Last Updated on STN: 15 Jun 2007
Entered Medline: 14 Jun 2007
AB Interleukin 4 receptor alpha (IL-4Ralpha) is essential for effective clearance of gastrointestinal nematode infections. Smooth

muscle cells are considered to play a role in the type 2 immune response-driven expulsion of gastrointestinal nematodes. Previous studies have shown in vitro that signal transducer and activator of transcription 6 signaling in response to parasitic nematode infection significantly increases smooth muscle cell contractility. Inhibition of the IL-4Ralpha pathway inhibits this response. How this response manifests itself in vivo is unknown. In this study, smooth muscle cell IL-4Ralpha-deficient mice (SM-MHC(Cre)IL-4Ralpha(-/lox)) were generated and characterized to uncover any role for IL-4/IL-13 in this non-immune cell type in response to Nippostrongylus brasiliensis infection. IL-4Ralpha was absent from alpha-actin-positive smooth muscle cells, while other cell types showed normal IL-4Ralpha expression, thus demonstrating efficient cell-type-specific deletion of the IL-4Ralpha gene. N. brasiliensis-infected SM-MHC(Cre)IL-4Ralpha(-/lox) mice showed delayed ability to resolve infection with significantly prolonged fecal egg recovery and delayed worm expulsion. The delayed expulsion was related to a delayed intestinal goblet cell hyperplasia, reduced T helper 2 cytokine production in the mesenteric lymph node, and reduced M3 muscarinic receptor expression during infection. Together, these results demonstrate that in vivo IL-4Ralpha-responsive smooth muscle cells are beneficial for N. brasiliensis expulsion by coordinating T helper 2 cytokine responses, goblet hyperplasia, and acetylcholine responsiveness, which drive smooth muscle cell contractions.

L4 ANSWER 15 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2006221948 EMBASE
TITLE: Chemical genetics reveals an RGS/G-protein role in the action of a compound.
AUTHOR: Fitzgerald, Kevin; Tertyshnikova, Svetlana; Cao, Jian; Carroll, Pamela; Dubaquie, Yves; Krystek Jr., Stanley R.; Lodge, Nicholas J.; Starrett, John; Stouch, Terry; Thalody, George; Zhang, Yongmei; Walker, Stephen G.; Cockett, Mark; Wardwell-Swanson, Judi; Ross-Macdonald, Petra (correspondence)
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Pennington, NJ, United States. Petra.RossMacdonald@bms.com
AUTHOR: Moore, Lisa; Bjerke, Lynn; Burley, Ben; Choy, Robert; Doberstein, Steve; Franke, Yvonne; Kopczynski, Jenny; Wayne, Honey; Kindt, Rachel M.
CORPORATE SOURCE: Exelixis Incorporated, South San Francisco, CA, United States.
AUTHOR: Korswagen, Hendrik; Plasterk, Ronald; Van Der Linden, Alexander
CORPORATE SOURCE: Hubrecht Laboratory, Centre for Biomedical Genetics, Utrecht, Netherlands.
SOURCE: PLoS Genetics, (Apr 2006) Vol. 2, No. 4, pp. 425-437. arn. e57.
Refs: 50
ISSN: 1553-7390 E-ISSN: 1553-7404
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jun 2006
Last Updated on STN: 2 Jun 2006

AB We report here on a chemical genetic screen designed to address the mechanism of action of a small molecule. Small molecules that were active in models of urinary incontinence were tested on the nematode

Caenorhabditis elegans, and the resulting phenotypes were used as readouts in a genetic screen to identify possible molecular targets. The mutations giving resistance to compound were found to affect members of the RGS protein/G-protein complex. Studies in mammalian systems confirmed that the small molecules inhibit muscarinic G-protein coupled receptor (GPCR) signaling involving G-αq (G-protein alpha subunit). Our studies suggest that the small molecules act at the level of the RGS/G-αq signaling complex, and define new mutations in both RGS and G-αq, including a unique hypo-adapation allele of G-αq. These findings suggest that therapeutics targeted to downstream components of GPCR signaling may be effective for treatment of diseases involving inappropriate receptor activation. .COPYRGT. 2006 Fitzgerald et al.

L4 ANSWER 16 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 4

ACCESSION NUMBER: 2006211738 EMBASE
TITLE: MAU-8 is a Phosducin-like Protein required for G protein signaling in C. elegans.
AUTHOR: Lacoste, Caroline; Barthaux, Veronique; Iborra, Cecile; Seagar, Michael; Erard-Garcia, Madeleine (correspondence)
CORPORATE SOURCE: INSERM UMR 641, Universite de la Mediterranee, Faculte de Medecine Secteur Nord, Boulevard Pierre Dramard, 13916 Marseille Cedex 20, France. garcia.m@jean-roche.univ-mrs.fr
SOURCE: Developmental Biology, (1 Jun 2006) Vol. 294, No. 1, pp. 181-191.
Refs: 45
ISSN: 0012-1606 CODEN: DEBIAO
PUBLISHER IDENT.: S 0012-1606(06)00140-0
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jun 2006
Last Updated on STN: 8 Jun 2006

AB The mau-8(qm57) mutation inhibits the function of GPB-2, a heterotrimeric G protein β subunit, and profoundly affects behavior through the Gαq/Gαo signaling network in C. elegans. mau-8 encodes a nematode Phosducin-like Protein (PhLP), and the qm57 mutation leads to the loss of a predicted phosphorylation site in the C-terminal domain of PhLP that binds the Gβγ surface implicated in membrane interactions. In developing embryos, MAU-8/PhLP localizes to the cortical region, concentrates at the centrosomes of mitotic cells and remains associated with the germline blastomere. In adult animals, MAU-8/PhLP is ubiquitously expressed in somatic tissues and germline cells. MAU-8/PhLP interacts with the PAR-5/14.3.3 protein and with the Gβ subunit GPB-1. In mau-8 mutants, the disruption of MAU-8/PhLP stabilizes the association of GPB-1 with the microtubules of centrosomes. Our results indicate that MAU-8/PhLP modulates G protein signaling, stability and subcellular location to regulate various physiological functions, and they suggest that MAU-8 might not be limited to the Gαq/Gαo network. .COPYRGT. 2006 Elsevier Inc. All rights reserved.

L4 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:594737 CAPLUS
DOCUMENT NUMBER: 143:226205
TITLE: TYRA-2 (F01E11.5): A Caenorhabditis elegans tyramine receptor expressed in the MC and NSM pharyngeal neurons
AUTHOR(S): Rex, Elizabeth; Hapiak, Vera; Hobson, Robert; Smith, Katherine; Xiao, Hong; Komuniecki, Richard

CORPORATE SOURCE: Department of Biological Sciences, University of Toledo, Toledo, OH, USA
SOURCE: Journal of Neurochemistry (2005), 94(1), 181-191 CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, a C. elegans tyramine receptor, SER-2, was identified that is involved in the tyramine (TA)-dependent regulation of these processes. In the present study, we have identified a 2nd C. elegans gene, tyra-2 (F01E11.5) that encodes a tyramine receptor. This is the 1st identification of multiple tyramine receptor genes in any invertebrate. Membranes from COS-7 cells expressing TYRA-2 bind [3H]tyramine with high affinity with a Kd of 20 nM. Other physiol. relevant biogenic amines, such as octopamine and dopamine, inhibit [3H]tyramine binding with much lower affinity (Kis of 1.55 and 1.78 μM, resp.), supporting the identification of TYRA-2 as a tyramine receptor. Indeed, tyramine also dramatically increases GTPγS binding to membranes from cells expressing TYRA-2 (EC50 of 50 nM) and the TA-dependent GTPγS binding is PTX-sensitive suggesting that TYRA-2 may couple to Gαi/o. Based on fluorescence from tyra::gfp fusion constructs, TYRA-2 expression appears to be exclusively neuronal in the MC and NSM pharyngeal neurons, the AS family of amphid neurons and neurons in the nerve ring, body, and tail. Taken together, these results suggest that TYRA-2 encodes a 2nd Gαi/o-coupled tyramine receptor and suggests that TA-dependent neuromodulation may be mediated by multiple receptors and more complex than previously appreciated.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 30 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004635716 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15610819
TITLE: Brief application of AF2 produces long lasting potentiation of nAChR responses in Ascaris suum.
AUTHOR: Trailovic Sasa M; Clark Cheryl L; Robertson Alan P; Martin Richard J
CORPORATE SOURCE: Department of Biomedical Sciences, Iowa State University, Ames, IA 50010, USA.
CONTRACT NUMBER: R01 A147194-02
SOURCE: Molecular and biochemical parasitology, (2005 Jan) Vol. 139, No. 1, pp. 51-64.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 22 Dec 2004
Last Updated on STN: 5 Aug 2005
Entered Medline: 4 Aug 2005
AB Resistance of parasitic nematodes to the cholinergic anthelmintic levamisole is associated with a reduction in the proportion of time that acetylcholine receptor ion-channels are in the open state decreasing the response of nematode parasites to the drug. Here we examine electrophysiological and contractile responses to acetylcholine and the cholinergic agonist, levamisole, in Ascaris suum muscle looking for a pharmacological approach that may be developed to increase the response to cholinergic agonists. We found that short application of the FMRFamide, AF2, produced modulation (long lasting potentiation) of the

peak membrane potential response to acetylcholine but not to levamisole. Since levamisole preferentially activates L-type acetylcholine receptors, we also tested the effect of nicotine (selective activator of N-type acetylcholine receptors) and bephenium (selective activator of B-type acetylcholine receptors) and found again no effect of AF2 on peak membrane potential responses. We then tested atropine on the AF2 potentiation of acetylcholine and found it to inhibit the peak potentiation suggesting that AF2 receptors interact with muscarinic receptors to produce the potentiation of acetylcholine. We saw similar atropine sensitive potentiation of acetylcholine responses in our muscle contraction experiments. The potentiation of the acetylcholine responses shows that nematode acetylcholine receptors are capable of a level of plasticity. A model involving calcium release from the sarcoplasmic reticulum, CaM Kinase, calcineurin, muscarinic receptors and AF2 receptors is proposed to explain our observations. These observations are important because they point to a pharmacological approach that may be developed to counter resistance to cholinergic anthelmintics.

L4 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:847051 CAPLUS
DOCUMENT NUMBER: 142:110702
TITLE: Activation of EGL-47, a Gαo-coupled receptor, inhibits function of hermaphrodite-specific motor neurons to regulate Caenorhabditis elegans egg-laying behavior
AUTHOR(S): Moresco, James J.; Koelle, Michael R.
CORPORATE SOURCE: Department of Genetics, Yale University School of Medicine, New Haven, CT, 06520, USA
SOURCE: Journal of Neuroscience (2004), 24(39), 8522-8530 CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB C. elegans egg-laying behavior is inhibited by neurotransmitter signaling through the neural G-protein Gαo and serves as a model for analyzing Gαo signaling. Mutations that alter egg-laying frequency have identified genes encoding a number of signaling proteins that act with Gαo, but the receptors that activate Gαo remain mostly uncharacterized. To further analyze Gαo signaling, we cloned the egl-47 gene, which was identified by 2 dominant mutations that severely inhibit egg laying. Egl-47 encodes 2 orphan G-protein-coupled receptor isoforms, which share all 7 transmembrane domains but have different extracellular N termini. Both dominant mutations change the same alanine to valine in the 6th transmembrane domain, resulting in constitutively activated receptors. Deletion of the egl-47 gene caused no detectable egg-laying defects, suggesting that EGL-47 functions redundantly, or it inhibits egg laying under specific circumstances as yet unidentified. Using promoter::green fluorescent protein transgenes, we found that EGL-47 is expressed in a number of neurons, including the hermaphrodite-specific neurons (HSNs) that innervate the egg-laying muscles to stimulate contraction. Transgenic expression of constitutively active EGL-47 or constitutively active Gαo specifically in the HSNs was sufficient to inhibit egg-laying behavior. Our results suggest that EGL-47 regulates egg laying by activating Gαo in the HSN motor neurons to inhibit their activity. Because several neurotransmitters act through Gαo to inhibit HSN function, it appears that loss of any 1 receptor, such as EGL-47, causes only mild defects. Gαo apparently integrates signaling from multiple receptors in the HSNs, including EGL-47, to set the frequency of egg-laying behavior.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:522283 CAPLUS
DOCUMENT NUMBER: 142:16258
TITLE: Phosphoinositide-3-OH-kinase inhibitor LY294002 prevents activation of Ancylostoma caninum and Ancylostoma ceylanicum third-stage infective larvae
AUTHOR(S): Brand, Andrea; Hawdon, John M.
CORPORATE SOURCE: Department of Microbiology and Tropical Medicine, The George Washington University Medical Center, Washington, DC, 20037, USA
SOURCE: International Journal for Parasitology (2004), 34(8), 909-914
CODEN: IJPYBT; ISSN: 0020-7519
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The developmentally arrested hookworm infective larva resumes development only after encountering specific host-mediated cues during invasion. These cues activate a signaling pathway that culminates in the resumption of development. In Ancylostoma caninum, activation is characterized by the resumption of feeding and the release of excretory/secretory products required for infection. The dauer stage of the free-living nematode Caenorhabditis elegans is a developmentally arrested stage analogous to the hookworm infective larva. Dauer larvae exit developmental arrest in response to environmental cues that indicate favorable conditions for reproduction and growth. Because of the similarity between dauer recovery and activation, exit from dauer provides a model for hookworm larval activation. An insulin-signaling pathway has been implicated in controlling exit from developmental arrest in both C. elegans dauers and A. caninum larvae. To further investigate the role of insulin signaling in hookworm larval activation, the phosphatidylinositol-3-OH kinase inhibitor LY294002 was tested for its effect on in vitro activation using the resumption of feeding as a marker for activation. LY294002 prevented feeding in A. caninum infective larvae stimulated with host serum filtrate and a glutathione-analog, the muscarinic agonist arecoline, or the cell permeable cGMP-analog 8-bromo-cGMP. Similar results were seen with the congeneric hookworm Ancylostoma ceylanicum. These data suggest that an insulin-signaling pathway mediates activation in hookworm larvae, as in C. elegans, and that the phosphatidylinositol-3-OH kinase inhibitor acts downstream of the cGMP and muscarinic signaling steps in the pathway. In A. caninum, LY294002 had no effect on the release of excretory/secretory products associated with activation, suggesting that the secretory pathway diverges from the activation pathway upstream of the phosphatidylinositol-3-OH kinase step. These results provide addnl. support for the insulin-signaling pathway as the primarily pathway for activation to parasitism in hookworm larvae.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:349381 CAPLUS
DOCUMENT NUMBER: 140:405367
TITLE: TLR-independent control of innate immunity in Caenorhabditis elegans by the TIR domain adaptor protein TIR-1, an ortholog of human SARM
AUTHOR(S): Couillault, Carole; Pujol, Nathalie; Reboul, Jerome; Sabatier, Laurence; Guichou, Jean-Francois; Kohara, Yuji; Ewbank, Jonathan J.
CORPORATE SOURCE: Centre d'Immunologie de Marseille-Luminy, Institut National de la Sante et de la Recherche

Medicale/Centre National de la Recherche Scientifique/Universite de la Mediterranee, Marseille, 13288, Fr.
SOURCE: Nature Immunology (2004), 5(5), 488-494
CODEN: NIAMCZ; ISSN: 1529-2908
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both plants and animals respond to infection by synthesizing compds. that directly inhibit or kill invading pathogens. We report here the identification of infection-inducible antimicrobial peptides in Caenorhabditis elegans. Expression of two of these peptides, NLP-29 and NLP-31, was differentially regulated by fungal and bacterial infection and was controlled in part by tir-1, which encodes an ortholog of SARM, a Toll-interleukin 1 receptor (TIR) domain protein. Inactivation of tir-1 by RNA interference caused increased susceptibility to infection. We identify protein partners for TIR-1 and show that the small GTPase Rab1 and the f subunit of ATP synthase participate specifically in the control of antimicrobial peptide gene expression. As the activity of tir-1 was independent of the single nematode Toll-like receptor, TIR-1 may represent a component of a previously uncharacterized, but conserved, innate immune signaling pathway.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:721964 CAPLUS
DOCUMENT NUMBER: 140:125452
TITLE: Genetic and cellular basis for acetylcholine inhibition of Caenorhabditis elegans egg-laying behavior
AUTHOR(S): Bany, I. Amy; Dong, Meng-Qiu; Koelle, Michael R.
CORPORATE SOURCE: Department of Cell Biology, Yale University School of Medicine, New Haven, CT, 06520, USA
SOURCE: Journal of Neuroscience (2003), 23(22), 8060-8069
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Egg-laying behavior in C. elegans is activated by signaling through the G-protein Gαq and inhibited by signaling through a 2nd G-protein, Gαo. Activation of egg laying depends on the serotonergic hermaphrodite-specific neurons (HSNs), but the neurotransmitter(s) and cell(s) that signal to inhibit egg laying are not known. Mutants for G-protein signaling genes have well characterized defects in egg laying. Here we present an anal. of mutants for other genes reported to lack inhibition of egg laying. Of the 9 strongest, 6 have morphol. defects in the ventral-type C (VC) neurons, which synapse onto both the HSNs and the egg-laying muscles and are thus the 3rd cell type comprising the egg-laying system. Laser-ablating VC neurons could also disrupt the inhibition of egg laying. The remaining 3 mutants (unc-4, cha-1, and unc-17) are defective for synthesis or packaging of acetylcholine in the VCs. The egg-laying defects of unc-4, cha-1, and unc-17 were rescued by VC-specific expression of the corresponding cDNAs. In addition, increasing synaptic acetylcholine by reducing acetylcholinesterase activity, with either mutations or the inhibitor aldicarb, decreased egg laying. Finally, we found that a knock-out for the HSN-expressed receptor G-protein-coupled acetylcholine receptor 2 (GAR-2) shows a partial defect in the inhibition of egg laying and fails to respond to aldicarb. Our results show that acetylcholine released from the VC neurons inhibits egg-laying behavior. This inhibition may be caused, in part, by acetylcholine signaling onto the HSN presynaptic terminals, via

GAR-2, to inhibit neurotransmitter release.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 30 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003514242 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14588249
TITLE: Serotonin and Go modulate functional states of neurons and muscles controlling C. elegans egg-laying behavior.
AUTHOR: Shyn Stanley I; Kerr Rex; Schafer William R
CORPORATE SOURCE: Program in Neurosciences, University of California, San Diego, La Jolla 92093, USA.
CONTRACT NUMBER: DA16445 (United States NIDA)
GM07198 (United States NIGMS)
SOURCE: Current biology : CB, (2003 Oct 28) Vol. 13, No. 21, pp. 1910-5.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 1 Nov 2003
Last Updated on STN: 24 Jan 2004
Entered Medline: 23 Jan 2004
AB From nematodes to humans, animals employ neuromodulators like serotonin to regulate behavioral patterns and states. In the nematode C. elegans, serotonin has been shown to act in a modulatory fashion to increase the rate and alter the temporal pattern of egg laying. Though many candidate effectors and regulators of serotonin have been identified in genetic studies, their effects on specific neurons and muscles in the egg-laying circuitry have been difficult to determine. Using the genetically encoded Ca(2+) indicator cameleon, we found that serotonin acts directly on the vulval muscles to increase the frequency of Ca(2+) transients. In contrast, we found that the spontaneous activity of the egg-laying motorneurons was silenced by serotonin. Mutations in G protein alpha subunit genes altered the responses of both vulval muscles and egg-laying neurons to serotonin; specifically, mutations in the G(q)alpha homolog egl-30 blocked serotonin stimulation of vulval muscle Ca(2+) transients, while mutations in the G(o)alpha homolog goa-1 prevented the silencing of motorneuron activity by serotonin. These data indicate that serotonin stimulates egg laying by directly modulating the functional state of the vulval muscles. In addition, serotonin inhibits the activity of the motorneurons that release it, providing a feedback regulatory effect that may contribute to serotonin adaptation.

L4 ANSWER 24 OF 30 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003266194 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12791979
TITLE: Wnt signaling, Ca2+, and cyclic GMP: visualizing Frizzled functions.
AUTHOR: Wang Hsien-Yu; Malbon Craig C
CORPORATE SOURCE: Department of Physiology and Biophysics, Health Sciences Center, State University of New York at Stony Brook, Stony Brook, NY 11794-8661, USA.
SOURCE: Science (New York, N.Y.), (2003 Jun 6) Vol. 300, No. 5625, pp. 1529-30.
Journal code: 0404511. E-ISSN: 1095-9203.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 8 Jun 2003
Last Updated on STN: 27 Jun 2003
Entered Medline: 26 Jun 2003

AB Wnts control the specification of cell fate, cell adhesion, migration, polarity, and proliferation. Their roles in development have been probed in fruit flies, nematodes, zebrafish, frogs, and mice. Some Wnts inhibit the degradation of beta-catenin, which can regulate transcription of specific genes. Other Wnts exert their influences in other ways, such as increasing intracellular concentrations of Ca2+ and decreasing intracellular concentrations of cyclic guanosine monophosphate (cGMP). Heterotrimeric guanine nucleotide-binding proteins (G proteins) and RGS proteins have been implicated in Wnt signaling. Wnt regulation of intracellular Ca2+ and cGMP levels requires the G protein transducin and a cGMP-specific phosphodiesterase, which are major elements in signaling of the visual pathway.

L4 ANSWER 25 OF 30 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:582326 BIOSIS
DOCUMENT NUMBER: PREV200300572161
TITLE: TGFbeta-INDUCED CHANGES IN MUSCARINIC RECEPTOR AFFINITY AND IN THE CONTRACTILITY OF INTESTINAL SMOOTH MUSCLE CELLS. .
AUTHOR(S): Akiho, Hirotada Jr. [Reprint Author]; Deng., Yikang; Collins, Stephen M.; City, Iizuka
CORPORATE SOURCE: Fukuoka, Japan
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. M1290. e-file. Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB BACKGROUND: Intestinal inflammation is accompanied by changes in smooth muscle contractility. In the murine model of intestinal inflammation due nematode infection, we observed an increase in the contractile response of muscle to the muscarinic agonist carbachol. This is due in part to the Th2 cytokines IL-4 and IL-13 which influence the muscarinic receptor. TGFb is also increased in the muscle layer in this model but its role in the model is unknown. AIM: In this study, we investigate the ability of TGFb to alter contractility of intestinal muscle. We investigate whether the TGFb receptor is present on muscle, and whether TGFb alters muscarinic receptor affinity and the contractility of murine intestinal smooth muscle cells. METHODS: Muscle cells were isolated by collagenase digestion from londitudinal muscle myenteric plexus (LMMP) that had been preincubated overnight with or without 10ng/ml of TGFb. TGFb and TGFb typeII receptor mRNA expression, muscle

contractility, and muscarinic receptor characteristics by agonist displacement of (N-methyl-3H) scopolamine ((3H)NMS) binding were examined. RESULTS: TGFb (543bp)mRNA expression was significantly increased in muscle from infected-mice compared to the control ($p<0.05$) and two distinct forms of mouse TGFb typeII receptor (526bp, 601bp) were expressed. Specific binding of (3H)-NMS was concentration dependent over a range of 0.1-10nM (3H)-NMS. Scatchard analysis revealed a dissociation constant (KD) for scopolamine of 2.6nM and a Bmax value of 2.4 ' 104 sites/cell. Preincubation of LMMP with TGFb increased the Bmax to 5.0 ' 104 sites/cell, ($p<0.01$) and enhanced carbachol-induced muscle contractility ($p<0.01$). Two agonist binding sites were identified in displacement experiments using carbachol; a low affinity site (KL) with an inhibitory constant (Ki) of 0.2mM and a high affinity site (KH) with a Ki of 4.1nM. Preincubation of LMMP with TGFb decreased the KH to 2.2pM. CONCLUSION: These results demonstrate that TGFb alters contractility of intestinal smooth muscle by increasing muscarinic receptor, and is a putative mediator of the hypercontractility observed during intestinal inflammation. Supported by Canadian Institute for Health Research..

L4 ANSWER 26 OF 30 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:194213 BIOSIS
DOCUMENT NUMBER: PREV200400194773
TITLE: Latrophilin activation by the novel anthelmintic emodepside stimulates vesicle release through a Galphaq, phospholipase - Cbeta, unc - 13 pathway.
AUTHOR(S): Willson, J. M. [Reprint Author]; Davis, A. [Reprint Author]; Harder, A.; Holden-Dye, L. [Reprint Author]; Walker, R. J. [Reprint Author]
CORPORATE SOURCE: Sch. of Biological Sci., Univ. of Southampton, Southampton, UK
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 122.3. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB The role of latrophilin receptors in the regulation of neurotransmitter release is unclear. Emodepside is a novel anthelmintic where the target site in nematodes appears to be a latrophilin-like receptor. Using the rhodamine dye FM4-64, which labels active synapses, emodepside was shown to stimulate vesicle release in C. elegans. We have used emodepside on the model organism Caenorhabditis elegans to provide a unique opportunity to define the signaling pathway of latrophilin-like receptors in C. elegans. In C. elegans two latrophilin-like genes have been identified; lat-1 (B0457.1) and lat-2 (B0286.2). We have shown that emodepside inhibits the activity of the pharyngeal muscle (IC50 4.1nM 95% confidence limits 0.79 to 21nM, n>3) and have used this as a bioassay to delineate the mechanism of action of this drug. RNAi to lat-1 resulted in 39 fold decreased sensitivity to emodepside (IC50=70nM, 95% confidence limits 22to219nM, n>3) indicating the mechanism of action for this anthelmintic primarily involves lat-1. Resistance in C. elegans lacking proteins required for vesicle fusion, namely UNC-13 (206 fold less sensitive, IC50= 360nM,95% confidence limits 68 to 1905nM, n>4), and synaptobrevin (29 fold less sensitive, IC50= 123nM, 95% confidence limits 33 to 460nM n>3), suggests the action of emodepside is pre-synaptic. We

investigated the signaling pathway through which emodepside may stimulate vesicle release. egl-30 (Galphaq) and egl-8 (Phospholipase-Cbeta) loss-of-function mutations both resulted in decreased sensitivity to emodepside, whereas egl-30 gain-of-function mutations resulted in hypersensitivity to emodepside. Taken together we propose that latrophilin receptor stimulation in C. elegans acts through Galphaq, PLC-beta, UNC-13 pathway to stimulate vesicle release.

L4 ANSWER 27 OF 30 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 8

ACCESSION NUMBER: 2002191089 EMBASE
TITLE: A Caenorhabditis elegans pheromone antagonizes volatile anesthetic action through a go-coupled pathway.
AUTHOR: Van Swinderen, Bruno; Metz, Laura B.; Shebester, Laynie D.; Crowder, C. Michael (correspondence)
CORPORATE SOURCE: Department of Anesthesiology, Box 8054, Washington Univ. School of Medicine, 660 S. Euclid Ave., St. Louis, MO 63110, United States. crowderm@morpheus.wustl.edu
SOURCE: Genetics, (2002) Vol. 161, No. 1, pp. 109-119. Refs: 56 ISSN: 0016-6731 CODEN: GENTAE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 2002
Last Updated on STN: 13 Jun 2002

AB Volatile anesthetics (VAs) disrupt nervous system function by an ill-defined mechanism with no known specific antagonists. During the course of characterizing the response of the nematode C. elegans to VAs, we discovered that a C. elegans pheromone antagonizes the VA halothane. Acute exposure to pheromone rendered wild-type C. elegans resistant to clinical concentrations of halothane, increasing the EC(50) from 0.43 ± 0.03 to 0.90 ± 0.02. C. elegans mutants that disrupt the function of sensory neurons required for the action of the previously characterized dauer pheromone blocked pheromone-induced resistance (Pir) to halothane. Pheromone preparations from loss-of-function mutants of daf-22, a gene required for dauer pheromone production, lacked the halothane-resistance activity, suggesting that dauer and Pir pheromone are identical. However, the pathways for pheromone's effects on dauer formation and VA action were not identical. Not all mutations that alter dauer formation affected the Pir phenotype. Further, mutations in genes not known to be involved in dauer formation completely blocked Pir, including those altering signaling through the G proteins Goα and Gqα. A model in which sensory neurons transduce the pheromone activity through antagonistic Go and Gq pathways, modulating VA action against neurotransmitter release machinery, is proposed.

L4 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:115722 CAPLUS
DOCUMENT NUMBER: 134:263707
TITLE: Notch inhibition of RAS signaling through MAP kinase phosphatase LIP-1 during C. elegans vulval development
AUTHOR(S): Berset, Thomas; Hoier, Erika Frohli; Battu, Gopal; Canevascini, Stefano; Hajnal, Alex
CORPORATE SOURCE: Division of Cancer Research, Department of Pathology,

University of zurich, Zurich, CH-8091, Switz.
SOURCE: Science (Washington, DC, United States) (2001), 291(5506), 1055-1058
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During Caenorhabditis elegans vulval development, a signal from the anchor cell stimulates the RTK/RAS/MAPK (receptor tyrosine kinase/RAS/mitogen-activated protein kinase) signaling pathway in the closest vulval precursor cell P6.p to induce the primary fate. A lateral signal from P6.p then activates the Notch signaling pathway in the neighboring cells P5.p and P7.p to prevent them from adopting the primary fate and to specify the secondary fate. The MAP kinase phosphatase LIP-1 mediates this lateral inhibition of the primary fate. LIN-12/NOTCH up-regulates lip-1 transcription in P5.p and P7.p where LIP-1 inactivates the MAP kinase to inhibit primary fate specification. LIP-1 thus links the 2 signaling pathways to generate a pattern.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:151265 CAPLUS
DOCUMENT NUMBER: 134:293057
TITLE: Two RGS proteins that inhibit Gαo and Gαq signaling in C. elegans neurons require a Gβ5-like subunit for function
AUTHOR(S): Chase, Daniel L.; Patikoglou, Georgia A.; Koelle, Michael R.
CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT, 06520, USA
SOURCE: Current Biology (2001), 11(4), 222-231
CODEN: CUBLE2; ISSN: 0960-9822
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gβ proteins have traditionally been thought to complex with Gγ proteins to function as subunits of G protein heterotrimers. The divergent Gβ5 protein, however, can bind either Gγ proteins or regulator of G protein signaling (RGS) proteins that contain a G γ-like (GGL) domain. RGS proteins inhibit G protein signaling by acting as Gα GTPase activators. While Gβ5 appears to bind RGS proteins in vivo, its association with Gγ proteins in vivo has not been clearly demonstrated. It is unclear how Gβ5 might influence RGS activity. In C. elegans there are exactly 2 GGL-containing RGS proteins, EGL-10 and EAT-16, and they inhibit Gαo and Gαq signaling, resp. We knocked out the gene encoding the C. elegans Gβ5 ortholog, GPB-2, to determine its physiol. roles in G protein signaling. The gpb-2 mutation reduces the functions of EGL-10 and EAT-16 to levels comparable to those found in egl-10 and eat-16 null mutants. Gpb-2 knockout animals are viable, and exhibit no obvious defects beyond those that can be attributed to a reduction of EGL-10 or EAT-16 function. GPB-2 protein is nearly absent in eat-16; egl-10 double mutants, and EGL-10 protein is severely diminished in gpb-2 mutants. Thus, Gβ5 functions in vivo complexed with GGL-containing RGS proteins. In the absence of Gβ5, these RGS proteins have little or no function. The formation of RGS-Gβ5 complexes is required for the expression or stability of both the RGS and Gβ5 proteins. Appropriate RGS-Gβ5 complexes regulate both Gαo and Gαq proteins in vivo.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:501925 CAPLUS
DOCUMENT NUMBER: 122:261482
ORIGINAL REFERENCE NO.: 122:47621a,47624a
TITLE: The Caenorhabditis elegans gene mek-2 is required for vulval induction and encodes a protein similar to the protein kinase MEK
AUTHOR(S): Kornfeld, Kerry; Guan, Kun-Liang; Horvitz, H. Robert
CORPORATE SOURCE: Dep. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139, USA
SOURCE: Genes & Development (1995), 9(6), 756-68
CODEN: GEDEEP; ISSN: 0890-9369
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An evolutionarily conserved signal transduction pathway that utilizes a receptor tyrosine kinase and a Ras protein mediates the induction of vulval cell fates in the nematode C. elegans. The authors sought new genes that function in this pathway by screening for suppressors of the Multivulva phenotype caused by a mutation that activates the let-60 ras gene. Seven such suppressor mutations defined a new gene involved in vulval induction. The authors named this gene mek-2, because its predicted protein product is most similar to MEK, a protein-serine/threonine and tyrosine kinase. Mek-2 mutations can be arranged in an allelic series. A probable null mutation eliminated vulval induction, and the strongest mutations alter codons conserved in most or all protein kinases. The genetic anal. showed that mek-2-functions downstream of let-60 ras and is required for ras-mediated signal transduction in vivo. The MEK-2 protein may interact with the products of the lin-45 raf and mpk-1 MAP kinase genes, which also mediate vulval induction.

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